

**METHODS OF TREATING DISORDERS RELATED TO APOE4**

**ABSTRACT OF THE DISCLOSURE**

[00240] The present invention provides methods inhibiting formation of neurofibrillary tangles; and methods for treating disorders relating to apolipoprotein E (apoE) in a subject. The methods generally involve reducing the level of a carboxyl-terminal truncated form of apoE in a neuronal cell of a subject. The invention further provides isolated cells comprising a nucleic acid molecule encoding a carboxyl-terminal truncated form of apoE; and methods of screening compounds using the cells. The invention further provides compounds that inhibit an apoE cleavage enzyme, and that reduce the formation of neurofibrillary tangles in a neuronal cell. The invention further provides transgenic non-human animals that include as a transgene a nucleic acid that encodes a carboxyl-terminal truncated form of apoE; as well as methods of screening compounds using transgenic animals.

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